REMARKS

Sequence Listings

Applicants request entry of this amendment in adherence with 37 C.F.R. §§1.821 to 1.825. The information contained in the computer readable form of Application No. 09/526,106 was prepared through the use of the software program "PatentIn" and is identical to that of the paper copy, a copy of which is enclosed for the convenience of the Examiner.

Claim Amendments

Claims 1-62 are herein canceled without prejudice. New claims 63-74 are added.

This preliminary amendment provides a new set of claims particularly pointing out that the fragment complementation system comprises two oligopeptides, each containing a Class A β-lactamase protein covalently bonded to an interactor domain ***through the Class A β-lactamase breakpoint***. Support for this claim element can be found throughout the specification, for example, at page 9, line 29 to page 10 line 3 (stating, "[t]he fragment pairs are used in methods that involve the co-expression of a first and a second oligopeptide sequence, in which the first oligopeptide sequence is a fusion protein comprised of in the direction of translation, an N-terminal fragment fused through a break-point terminus to a flexible polypeptide linker and a first interactor domain, and the second oligopeptide sequence is a fusion protein comprised of in the direction of translation, a second interactor domain and a flexible polypeptide linker fused through a break-point terminus to a C-terminal fragment."), and Examples 1-4, 6-9, and 11.

Claim 64 recites that the first oligopeptide and the second oligopeptide contain a signal peptide. Support for claim 64 can be found, for example, on page 11, lines 2-5 (stating "[f]or evaluating interactions between extracellular proteins, the first and second fusion oligopeptides can be expressed with a signal peptide. In bacterial host cells, for example, an N-terminal signal peptide can provide for translocation of the fusion oligopeptides to the periplasm"), and Examples 1-4, 6-9, and 11.

Claim 65 recites that the breakpoints are within 10 amino acids in either direction from a junction between 2 amino acid residues within a loop between elements of secondary

structure. Support for claim 65 can be found, for example, at page 13, lines 16-19 (stating "[t]he invention also provides for efficient methods of identifying functional fragment pairs of a marker protein of interest that involves preparing a multiplicity of fragment pair members with break-point termini within a solvent exposed loop or a flexible loop defined by tertiary or secondary structure analysis to obtain a fragment pair library") and at page 16, lines 25-28 (stating, "[t]he combined lengths of the fragment pairs may be discontinuous or overlapping, however, comprising from 90% to 110% of the total length of the parent protein, and the actual break-point could be within ten amino acid residues in either direction from an identified functional contiguous break-point junction.").

Claim 68 recites that the fragment complementation system further contains a peptide that enhances the functional reconstitution of the N-terminal fragment. Claim 70 specifies that the peptide is covalently bonded to the active site of a thioredoxin protein. Support for claim 68 and 70 may be found in the specification, for example, on page 11, lines 11-22 (stating, in part, "[t]he subject invention provides for enhancing the performance of the reassembled parent protein by introducing . . . a randomly-encoded peptide of 3-12 amino acids expressed separately as a fusion to the N-terminus of a thioredoxin with an intervening flexible linker.").

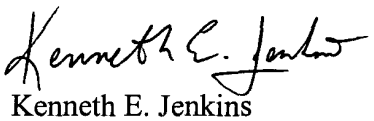
Claim 71 recites that the first and second oligopeptides further contain polypeptide linkers. Support for claim 71 can be found, for example, on page 10, lines 3-12 (stating, "[t]he flexible polypeptide linker separates the fragment domain from the interactor domain and allows for their independent folding. The linker is optimally 15 amino acids or 60 Å in length (~4 Å per residue) but may be as long as 30 amino acids but preferably not more than 20 amino acids in length. It may be as short as 3 amino acids in length, but more preferably is at least 6 amino acids in length.").

Claim 72 recites that the first and second oligopeptides further contain complementation enhancement peptides. Claims 73 and 74 recite specific sequences for the complementation enhancement peptides. Support for the sequences can be found, for example, at Example 6, page 44, line 14, to page 47, line 9 (stating, in part, "[a]nother way to enhance interaction-dependent enzyme fragment complementation is to introduce short, random peptide sequences at the break-points, and then to select for increased activity with a model interaction ... Synthetic oligonucleotides were used to add three randomized residues to each fragment between the break-point residue and the linker for the heterologous domain.").

In light of the above exemplary disclosures, Applicants assert that no new matter is added with this amendment.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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